Control of sodium and water balance
Regulation of plasma volume and osmolarity

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ILOs

By the end of this lecture the student should be able to:

I. Describe the renal mechanisms for sodium regulation:
   - Regulation of amount filtered.
   - Regulation of amount reabsorbed.

II. Describe the renal mechanisms for water regulation:
   - Role of osmoreceptors.
   - Role of baroreceptors.
   - Thirst.

Fluid balance is maintained by:

1) Control of extracellular fluid (ECF) osmolarity.
2) Control of ECF volume

1. *ECF osmolarity* must be closely regulated to *prevent swelling or shrinking of cells.* Maintaining *water balance* is of primary importance in regulating ECF osmolarity.

2. *ECF volume* must be closely regulated to help *maintain blood pressure.* Maintaining *salt balance* is of primary importance in the long-term regulation of ECF volume.

Control of ECF osmolarity (defense of tonicity):

- The total body osmolarity is directly proportional to the total body sodium plus the total body potassium divided by the total body water.
- So, changes in the osmolarity of the body fluids occur when a mismatch exists between the amount of these electrolytes and the amount of water ingested or lost from the body.

- Any circumstance that results in a loss or gain of *free* H_2O that is not accompanied by comparable solute deficit or excess leads to changes in ECF osmolarity.
- ECF osmolarity = 280-300 mOsm/L

Mechanisms for control of ECF osmolarity:
Are the mechanisms that control water balance:
1) ADH (vasopressin) secretion mechanism
2) Thirst mechanism

I. When ECF osmolarity increases (hypertonicity):
It is decreased towards normal level as follows:
Increase in osmolarity stimulates osmoreceptors in the anterior hypothalamus that causes two effects:

- Stimulation of secretion of ADH.
- Stimulation of thirst, which causes drinking behavior.

a. Increased secretion of ADH
from the posterior pituitary which produces an increase in water permeability of the principal cells of the distal tubule and collecting duct in kidney resulting in increased water reabsorption (via V_2 receptors) causing decreased urine volume.

b. Increased thirst sensation:
by stimulating thirst center in the hypothalamus that increases water intake.

II. When ECF osmolarity decreases (hypotonicity)
It is increased towards normal level by:
a. Decreased secretion of ADH causes increase of excretion of solute free water in urine.
b. Decreased thirst sensation due to deficient stimulation thirst center.

Control of ECF volume (defense of volume):

- The amount of Na^+ in the ECF is the most important determinant of ECF volume.
- An increase in the amount of Na^+ in the body salt in the ECF causes more H_2O in the ECF resulting in increased ECF volume, blood volume, and blood pressure. Conversely, a reduced salt load leads to decreased H_2O

retention, so the ECF volume, blood volume, and blood pressure are reduced.

- Regulation of ECF volume depends primarily on controlling salt (Na^+) balance.
- The kidneys excrete the excess salt in the urine to maintain salt balance.

The renal mechanisms for sodium regulation:

I. Regulation of amount filtered.
II. Regulation of amount reabsorbed.

I. Regulation of amount filtered:

The amount of Na^+ *filtered is controlled by regulating the GFR.*

At any given plasma Na^+ concentration, any change in the GFR will correspondingly change the amount of Na^+ that is filtered.

Thus, control of the GFR can adjust the amount of Na^+ filtered each minute.

Decreased Na^+ load → decrease ECF volume → decrease in blood pressure → decreases GFR → decreases the amount of Na^+ filtered → decreases the Na^+ excretion→ conservation of Na^+ and vice versa.

II. Regulation of amount reabsorbed:

The renal mechanisms that regulate Na^+ *reabsorption and thus excretion include:*

1. Starling forces in peritubular capillaries
2. Renin-angiotensin-aldosterone system
3. Sympathetic nerve activity
4. Atrial natriuretic peptide [ANP]

1. Starling forces in peritubular capillaries

When ECF volume is increased, the plasma protein concentration is decreased by dilution (osmotic pressure decreases) and the hydrostatic pressure within the peritubular capillaries increases resulting in decrease proximal tubule Na^+ reabsorption and enhanced urinary sodium excretion.

Conversely, when ECF volume is decreased, the plasma protein concentration is increased (osmotic pressure increases) and the hydrostatic pressure within the peritubular capillaries decreases resulting in increased proximal tubule Na^+ reabsorption and decreased urinary sodium excretion.

2. Renin-Angiotensin-Aldosterone System (RAAS)

Decreased ECF volume → decrease in blood volume and arterial blood pressure → decreased renal perfusion pressure → renin is released from juxtaglomerular cells and acts on angiotensinogen → angiotensin I, which is converted by angiotensin converting enzyme → angiotensin II which helps increasing ECF volume by causing sodium and water retention by the following effects:

- Vasoconstriction.
- Acts directly on the proximal tubule to enhance sodium reabsorption.
- Stimulates secretion of aldosterone from adrenal gland stimulates Na^+ reabsorption in the distal convoluted tubule and the collecting duct.
- Stimulates ADH secretion that increases water reabsorption causing increased ECF volume.
- Stimulates thirst center.
- Contraction of mesangial cells → decrease GFR.

3. Sympathetic nerve activity

Renal sympathetic nerve is activated by the baroreceptor mechanism in response to hypovolemia and decrease in arterial pressure and causes:

- Vasoconstriction of afferent arterioles causing decrease in RBF and GFR.
- Increase sodium reabsorption in the proximal tubule.
- Activation of the Renin-Angiotensin-Aldosterone System.

These sympathetic effects result in increased ECF volume serving to maintain arterial pressure in case of sudden large blood loss.

4. Atrial natriuretic peptide (**ANP**)

ANP is secreted by the atria in to increase in ECF volume.

ANP act on the kidneys to increase Na^+ excretion (natriuresis) by:

- dilating afferent arterioles and relaxing mesangial cells, both increase GFR
- decreasing Na^+ reabsorption in the late distal tubule and collecting ducts.
- inhibition of secretion of renin, aldosterone and ADH.

Role of baroreceptors

Although the major stimulus for vasopressin secretion and thirst is an increase in ECF osmolarity, the vasopressin-secreting cells and thirst center are both influenced by changes in ECF volume and blood pressure which are detected by cardiopulmonary baroreceptors (volume receptors) and arterial baroreceptors respectively.

i. Cardiopulmonary baroreceptors:
are stretch receptors in the low pressure regions (great veins, right and left atria, and pulmonary vessels). These volume receptors respond to fullness of vascular system or central venous pressure, which reflects the ECF volume.

ii. Arterial baroreceptors:
are stretch receptors in high pressure regions of the circulation; the aortic arch and carotid sinus. These pressure receptors monitor the mean driving pressure in the vascular system (detect arterial blood pressure).

- In response to major reduction in ECF volume (> 7% loss of volume) and in arterial pressure, as during hemorrhage, the decreased stimulation of high- pressure and low-pressure baroreceptors results in stimulation of both vasopressin secretion and thirst.
- (By comparison, the hypothalamic osmoreceptors have greater influence than the left atrial volume receptors in controlling vasopressin secretion and thirst because a change as small as a 1% increase in ECF osmolarity triggers increased vasopressin secretion, and an increase in osmolarity of 2-3% produces a strong desire to drink).

Whenever ECF volume decreases:
→ Decrease in arterial blood pressure
→ Decrease rate of discharge from these receptors
→ 1. Stimulation of ADH secretion and increasing thirst
2. Increasing sympathetic nervous system activity

Control of ECF volume
I. When ECF volume decreases:
It is increased towards normal level by:
Increasing retention of Na^+ and water and decreasing their urinary excretion by:

1. Decreasing GFR
2. Decreasing ANP and related peptides secretion
3. Decreasing discharge from high- pressure and low-pressure baroreceptors → increased sympathetic nervous system activity and increased thirst and ADH secretion.
4. Activation of renin angiotensin aldosterone system

5. Concentration of plasma protein which increases osmotic pressure and stimulates proximal tubule Na^+ reabsorption

II. When ECF volume increases:

It is decreased towards normal level by:

Increasing urinary excretion of Na^+ and water and decreasing their retention by:

1. Increasing GFR
2. Increasing ANP and related peptides secretion
3. Increasing discharge from high- pressure and low-pressure baroreceptors → decreased sympathetic nervous system activity and decreased thirst and ADH secretion.
4. Inactivation of renin angiotensin aldosterone system
5. Dilution of plasma protein which decreases osmotic pressure and inhibits proximal tubule Na^+ reabsorption